

Assessing risk with increasingly stringent public health goals: the case of water lead and blood lead in children

Simoni Triantafyllidou, Daniel Gallagher and Marc Edwards

ABSTRACT

Previous predictions of children's blood lead levels (BLLs) through biokinetic models conclude that lead in tap water is not a primary health risk for a typical child under scenarios representative of chronic exposure, when applying a 10 µg/dL BLL of concern. Use of the US Environmental Protection Agency Integrated Exposure Uptake Biokinetic (IEUBK) model and of the International Commission on Radiological Protection (ICRP) biokinetic model to simulate children's exposure to water lead at home and at school was re-examined by expanding the scope of previous modeling efforts to consider new public health goals and improved methodology. Specifically, explicit consideration of the more sensitive population groups (e.g., young children and, particularly, formula-fed infants), the variability in BLLs amongst exposed individuals within those groups (e.g., more sensitive children at the upper tail of the BLL distribution), more conservative BLL reference values (e.g., 5 and 2 µg/dL versus 10 µg/dL) and concerns of acute exposure revealed situations where relatively low water lead levels were predicted to pose a human health concern.

Key words | acute, biokinetic model, chronic, distribution, reconstituted formula, variability

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INTRODUCTION

Lead in tap water and lead in children's blood

Plumbing materials containing lead (lead pipe, lead solder, brass and bronze plumbing components) may contaminate drinking water at the tap. In the USA, a mandatory lead action level of 15 µg L⁻¹ has been set for home taps and a voluntary lead standard of 20 µg L⁻¹ has been set for school taps/fountains (US EPA 1991, 1991a). Drinking water has typically been considered a secondary exposure source, accounting for up to 20% of total lead exposure nationally (US EPA 1991a), with deteriorating lead paint and contaminated dust/soil being the primary lead sources (Levin et al. 1999).

In the past, although no levels of blood lead were deemed safe, the US Centers for Disease Control and Prevention (US CDC) considered 10 µg/dL as the blood lead level (BLL) of concern in children, elevations above which (i.e., elevated blood lead, EBL) cause detectable mental impairment and behavioral changes (US CDC 1991). The

CDC recently determined that lead in drinking water has been associated with US children's EBL or with BLLs that are higher than the geometric mean BLL (i.e., BLLs >1.4 µg/dL) (US CDC 2014a). A recent literature review also highlighted several cases where contaminated tap water was a major contributor to the BLL of US children, and further summarized epidemiological studies in the UK, Germany, France, and Canada indicating that elevated lead in water can similarly contribute to children's BLLs elsewhere (Triantafyllidou & Edwards 2014).

Biokinetic models for BLL predictions in children

To explore relationships between environmental lead and blood lead of exposed children, biokinetic models are frequently used for supporting risk assessment decisions when BLL data are not available (Pounds & Leggett 1999). Three biokinetic models have been commonly used in previous research to predict BLLs from exposure to lead in

water and other environmental media: (1) the US Environmental Protection Agency (US EPA) Integrated Exposure Uptake Biokinetic (IEUBK) model for lead in children (White et al. 1994; US EPA 1994); (2) the International Commission on Radiological Protection (ICRP) model for lead in children and adults, also called the Leggett model (Leggett 1984); and (3) the O'Flaherty model for lead in children and adults (O'Flaherty 1984). Evaluations/comparisons among the three models are available elsewhere (US EPA 1994b; Equilibrium Environmental Inc. 1994).

From these models, the IEUBK can additionally assess variability in predicted blood lead concentrations among children exposed to the same lead dose, by assuming log-normality of predicted BLLs with a geometric standard deviation (GSD) of 1.6 µg/dL around the predicted geometric

mean BLL (US EPA 1994). This variability reflects differences among children due to genetics and diets that result in a different individual response (i.e., different BLL) to the same lead dose.

Previous risk assessments

Previous modeling research of health risks from lead in tap water (Table 1) has been limited. This research concluded that lead in tap water is not a primary concern for a typical child under representative scenarios of chronic exposure, when applying the 10 µg/dL BLL of concern. For example, an IEUBK modeling approach which assessed lead exposure from tap water at an Australian home (Table 1) concluded that unless a typical child consumed water at

Table 1 | Summary of previous work on the modeling of children's BLL due to lead-contaminated drinking water and key conclusions

Previous work	Gulson et al. (1997)	Sathyanarayana et al. (2006)
Goal	Health risk assessment from elevated lead in water at a worst-case Australian home	Health risk assessment from elevated lead in water at 71 elementary schools in Seattle in 2004
Group(s) considered	Children aged 0.5–7 years, consuming all their water at home	Children aged 5–6 years, consuming half their water at a given school and half at home
Model used	EPA Integrated Exposure Uptake Biokinetic Model for Lead in Children (EPA IEUBK)	
Model inputs	WLL daily profile (as measured in the home): 100 µg/L first-draw, 46 µg/L daily average Model default values for other background lead exposures (outdoor air, indoor air, outdoor soil, indoor dust and dietary intake)	WLLs from 71 elementary schools in Seattle obtained from Seattle Public Schools' website pre-remediation: 1–1,600 µg/L First Draw, 1–370 µg/L Second Draw WLLs at home assumed fixed at 10.3 µg/L based on lead and copper rule sampling Soil lead content of 24 µg/g (as measured in Seattle) and model default values for other background lead exposures
Model outputs	Geometric mean BLL of children at the sampled home	Geometric mean BLL of children at each school
Scenarios considered	Five WLLs at home: 4 µg/L (IEUBK default value) 46 µg/L, 50% first draw 46 µg/L, 100% first draw 100 µg/L, 50% first draw 100 µg/L, 100% first draw	50% of water consumed at a given school and 50% consumed at home: 'Worst-case': Exposure to 90th percentile lead-in-water concentration at a given school 'Typical Case': Exposure to median lead-in-water concentration at that school (i.e., 50th percentile)
Key predictions and conclusions	Children aged 1–2 years had geometric mean BLLs \leq 10 µg/dL only when 100% of the consumed water contained 100 µg/L lead Hypothesized that if more than 0.5 L of first-flush water was consumed, by formula-fed infants or pregnant women, then the BLL would easily exceed the recommended level	Geometric mean BLLs < 10 µg/dL in all cases Drinking water exposures up to 10–15 times the EPA guideline are unlikely to result in EBL In Seattle, elevated school drinking water lead concentrations are not a significant source of lead exposure in school-age children Further analysis needed only if water lead concentrations far exceed the EPA recommendations by ~80–100 times

lead concentrations of approximately 100 µg/L, the BLL would not exceed the CDC's 10 µg/dL level of concern (Gulson et al. 2004). IEUBK modeling of BLLs in students in Seattle (USA) exposed to high lead in school water (Table 1) also concluded that drinking water does not significantly contribute to high BLLs in children (Sathyanarayana et al. 2004).

Children's lead exposure and risk assessment considerations as they affect predictive BLL modeling

Significant new research/policies and risk assessment considerations are explained below, which make it desirable to expand on the scope of previous modeling efforts.

Public health concern and public sensitivity over lower-level lead exposure

Although BLLs below 10 µg/dL in children are often considered 'normal,' they are nonetheless associated with intellectual deficits (Lanphear et al. 2004). In fact, evidence of neurodegenerative, cardiovascular, renal, and reproductive effects at BLLs under 10 µg/dL, and as low as 1–2 µg/dL have recently been summarized in the literature (Health Canada 2004). The European Union Risk Assessment Report recently proposed 5 µg/dL as an epistemic BLL threshold for impacts of lead upon societal cognitive resources, and 1.2 µg/dL as a reference point for the risk characterization of lead when assessing intellectual deficits in children measured by the full scale intelligence quotient (IQ) score (EUSCHER 2004). The US CDC also recently adopted a reduced 'BLL reference value' of 5 µg/dL (US CDC 2004b), lowering the previous 'BLL of concern' which had been used in previous modeling efforts (e.g., in Gulson et al. 2004; Sathyanarayana et al. 2004). The new reference value is based on the 97.5th percentile of the BLL distribution among surveyed children 1–5 years old in the USA (US CDC 2004b).

Risk assessment and public health policy target high-risk children (more sensitive or more exposed)

Significant progress has already been made in addressing EBL for large percentages of the population (US CDC 2004b). The

CDC therefore recognizes the need to identify and protect high-risk ends of the population distributions from environmental contaminants, including both the most sensitive and the most exposed individuals. The US Department of Health and Human Services has set the goal of eliminating every single instance of EBL in children as part of its 'Healthy People 2020' initiative (US DHHS 2004), and the CDC has also committed to that goal (US CDC 2004c).

Such objectives increase the importance of identifying and addressing all potential lead sources especially in sensitive subpopulations. For example, infants consuming reconstituted formula are considered a high-risk group, because tap water may account for more than 85% of their total lead exposure (US EPA 2004). In addition, variations in genetics and diets produce a range of BLLs in a population in response to a fixed lead dose (US EPA 2004). The few modeling efforts to assess water lead risks conventionally focused on the typical child through prediction of the geometric mean BLL (corresponding to the 50th percentile of the BLL distribution if the distribution is log-normal). They did not explicitly consider the response of more sensitive subpopulations (i.e., the 90, 95 or 99th percentile BLL in hypersensitive children drinking the same water dose) or more exposed subpopulations (i.e., formula-fed infants who consume greater water volumes). The IEUBK model allows for both considerations.

Acute health risk from lead exposure

After two cases of severe lead-poisoning by accidental ingestion of lead-containing jewelry charms, one of which was fatal (US CDC 2004, 2004), the US Consumer Product Safety Commission (CPSC) established 175 µg of lead in a piece of jewelry as a dose triggering acute health concerns, product recalls and fines, resulting in recalls of more than 150 million children's jewelry pieces in 2004 alone (US CPSC 2004). In this work, it is considered reasonable that a similar dose of lead through water (a product intended for human consumption) would also be cause for acute health concern. No previous studies of lead-in-water hazards have explicitly considered acute health risks in children. The ICRP allows simulating 1-day exposures through the model inputs, as opposed to 1-year chronic exposures considered in the IEUBK model (US EPA 2004), and 1-month exposures

considered in the recent IEUBK batch run mode (Donohue et al. 2004).

The goal of this work was to revisit previous modeling efforts by expanding their analyses to reflect these additional considerations. Such risk assessment considerations are not limited to these previous cases (listed in Table 1). The current work includes considerations that broadly apply to childhood lead exposure from water at school or at home in the USA and around the world, by attempting to better quantify health risks to children from this recognized lead source.

MATERIALS AND METHODS

Model simulations

The IEUBK model (win32 Version 1.1 build 9) was downloaded from the US EPA website at <http://www.epa.gov/superfund/lead/products.htm>. The ICRP model (version 3000, Microsoft Excel interface) was provided by the Syracuse Research Corporation.

IEUBK model simulations were undertaken to expand on the work of the following:

- (1) Gulson et al. (2004) on the IEUBK modeling of children's BLLs from water exposure at home (Table 2).
- (2) Sathyanarayana et al. (2006) on the IEUBK modeling of children's BLLs from water exposure at a given school (Table 2). First-draw and second-draw water lead levels (WLLs) as reported by Seattle Public Schools (2004) were used for this analysis.

In both cases, water lead inputs were altered from the IEUBK model default of 4 µg/L in order to represent actual water lead measurements at those locations (see Table 2). Because other environmental media (e.g., air, soil, dust, diet) were not the primary focus of this study, model default values were used to represent lead levels in those environmental media (US EPA 2004): outdoor air at 0.10 µg/m³ (indoor air at 30% of outdoor air), outdoor soil at 200 µg/g, indoor dust at 200 µg/g, and dietary intake at 1.95–2.26 µg/day (depending on age).

In addition to the chronic simulations of the IEUBK model (Table 2), the ICRP model was also utilized to simulate hypothetical scenarios of acute lead exposure from tap water in children.

Details for each of the three analyses follow.

Table 2 | Expanded modeling analyses undertaken in the present study to extend the scope of previous work to reflect modern public health goals for lead

Additional analysis (present work)	Motivated by Gulson et al. (1997)	Motivated by Sathyanarayana et al. (2006)
Extend previous goal to assess	Output variability in children's response to a fixed lead dose (post facto application of the default GSD in IEUBK model) Health impacts in more exposed population (formula-fed infants) Lower BLL cutoff values of 5, 2, and 1 µg/dL	Input variability in WLLs at a given school, by evaluating specific quantiles of the observed WLL (not just 50 and 90th percentile) Lower BLL cutoff of 5 µg/dL Output variability in children's response to a fixed lead dose (post facto application of the default GSD in IEUBK model)
Model water lead inputs	100 µg/L WLL (worst-scenario of previous work) and other WLLs Higher water consumption for formula-fed infants, compared to model default	Variable WLLs (one fixed input at a time) from different fountains of one elementary school Inclusion of actual worst-case exposure to 100% percentile lead-in-water concentration
Model used	EPA IEUBK	
Model predictions	Distribution of BLL with emphasis on upper tail that reflects the most sensitive children, not just geometric mean (i.e., 50th percentile BLL) that reflects the typical child Percent of children with EBL at each BLL cutoff value, as a risk assessment criterion	Distribution of BLL with emphasis on upper tail, not just geometric mean that reflects typical child Percentage of school children with EBL as a risk assessment criterion, not just geometric mean BLL

Biokinetic modeling of children's BLLs from chronic water exposure at home

The IEUBK modeling undertaken by Gulson et al. (2004) (see Table 1) was expanded by the following (Table 2):

Considering the whole distribution of predicted BLL with emphasis on the upper tail (75, 90, 95 and 99th percentile of predicted BLL), and not just the geometric mean. While the geometric mean BLL reflects the potential health impact for average children, the upper tail of the BLL distribution reflects the more sensitive children within a given age group, due to individual genetic and dietary factors affecting lead uptake and biokinetics. Considering lower BLLs, aside from the conventional 10 µg/dL BLL of concern. Specifically, 5 µg/dL, 2 µg/dL, and 1 µg/L were examined, consistent with the lower BLLs recently proposed by the US CDC or the EU Scientific Committee on Health and Environmental Risks.

Considering scenarios of formula-fed infants, consuming much higher volumes of water through reconstituted formula milk, compared to school-aged children drinking the water. Specifically, water consumption of 800 mL/day for 0–1-year-old infants relying on baby formula is considered average (US EPA 2000; EU SCHER 2000), whereas 1,200 mL/day is considered high (Benelam & Wyness 2000; EU SCHER 2000). The default daily water consumption for children who rely on water for direct consumption only, is set at a much lower volume of 200–590 mL/day in the IEUBK model, depending on age (US EPA 2000).

Biokinetic modeling of children's BLLs from chronic water exposure at schools

The IEUBK modeling undertaken by Sathyanarayana et al. (2004) (see Table 1) was expanded by the following (Table 2):

Considering the whole distribution of observed WLL and corresponding predicted BLL. This approach allows estimation of the percentage of the population that is predicted to have EBL (i.e., BLL \geq 10 µg/dL or more recently \geq 5 µg/dL) due to consumption of water

from different water fountains, and due to different individual patterns of lead uptake and biokinetics (US EPA 2000).

Biokinetic modeling of children's BLLs from acute water exposure

Previous modeling efforts that utilized the IEUBK model (Gulson et al. 2004; Sathyanarayana et al. 2004) assessed chronic scenarios of lead-in-water exposures in children, encompassing the model output time step of 1-year. From the three available biokinetic models for lead in children (IEUBK, ICRP, O'Flaherty), the ICRP incorporates a daily exposure input and can thus allow exploration of short-term lead exposures. ICRP modeling was undertaken to explore hypothetical scenarios of acute lead exposure through drinking water in children aged 5 years by the following:

Predicting BLL from direct consumption of a single glass of water (250 mL) containing various levels of lead (0–5,000 µg/L). The higher levels of lead (in the order of hundreds, or thousands µg/L) have been reported in some US field investigations, mostly comprised of particulate lead (Triantafyllidou & Edwards 2000). Aside from this one-time ingestion of the contaminated water, all lead exposures (from soil, air, food, water) were assumed to be equal to zero.

Predicting BLL from indirect consumption of the contaminated water, through consumption of one portion of pasta cooked with the water (750 mL of water required for one portion) containing various levels of lead (0–5,000 µg/L). Aside from this one-time ingestion of the contaminated food, all lead exposures (from soil, air, food, water) were assumed to be equal to zero. This scenario recognizes the potential for sorption of lead in food during cooking with large contaminated volumes (Moore 2000). Specifically, concentration of the lead into food via adsorption (up to 83% lead absorption from water into pasta) has been demonstrated in one experimental study (Smart et al. 2000), while this exposure pathway was recently implicated as the source of lead poisoning of two children in the USA (Copeland 2000; Triantafyllidou & Edwards 2000).

RESULTS AND DISCUSSION

Biokinetic modeling of children's BLLs from chronic water exposure at home

Utilizing the IEUBK model, Gulson et al. (2003) predicted that constant exposure to a WLL of about 100 µg/L (corresponding to first-draw water in a sampled Australian home), resulted in exceedance of the BLL of concern for a typical 1–2-year-old child (i.e., predicted geometric mean BLL > 10 µg/dL) (see Table 1). The authors qualified this conclusion by stating that if more water was consumed in drinks and formula using first-draw water, then the BLL could easily exceed the recommended level (Gulson et al. 2003). When the IEUBK modeling work of Gulson et al. (2003) for children aged 1–2 years was reproduced, a water lead level of 100 µg/L was indeed required in order for the

geometric mean BLL to exceed the 10 µg/dL BLL of concern (Table 3, scenario 1). Stated another way, at a WLL of 100 µg/L, 50% of the exposed children are predicted to develop EBL (i.e., BLL \geq 10 µg/dL).

Children's BLL sensitivity from chronic exposure and lower BLLs

The extended analysis performed herein reveals that a lower WLL of 55 µg/L is sufficient to elevate lead in blood (\geq 10 µg/dL) in 25% of the exposed children, whereas a WLL of 19 µg/L would be sufficient to elevate lead in blood in 5% of those children (Table 3, scenario 1). Children belonging to these percentiles (i.e., 25, 10, 5 and 1% in Table 3) reflect more sensitive children within the population of children, in comparison to the median response of a typical child (expressed by the 50th percentile in Table 3).

Table 3 | Required level of lead in water for a given percentile of exposed children to exceed certain BLL cutoff values. Predictions obtained with IEUBK model under three exposure scenarios, with assumptions listed for each scenario

BLL cutoff value (µg/dL)	Predicted WLL required to exceed BLL cutoff value for:				
	50th percentile (50% exceed BLL)	75th percentile (25% exceed BLL)	90th percentile (10% exceed BLL)	95th percentile (5% exceed BLL)	99th percentile (1% exceed BLL)
SCENARIO 1: 1–2-year-old child drinking tap water					
Assumptions: 500 mL/day water consumption (IEUBK default value)					
GSD $\frac{1}{4}$ 1.6 µg/dL (IEUBK default value)					
Background exposures from other lead sources set to IEUBK default values					
10	100 µg/L ^a	55 µg/L	30 µg/L	19 µg/L	3 µg/L
5	24 µg/L	7 µg/L	0 µg/L ^b	0 µg/L ^b	0 µg/L ^b
SCENARIO 2: 0–1-year-old infant consuming reconstituted baby formula, average consumption					
Assumptions: 800 mL/day water consumption [EPA (2003); average consumption in EU SCHER (2003)]					
GSD $\frac{1}{4}$ 1.45 µg/dL [EPA (2003) for formula-fed children]					
Exposure through diet set to 0					
Background exposures from other lead sources set to IEUBK default values					
10	60 µg/L	40 µg/L	28 µg/L	22 µg/L	13 µg/L
5	18 µg/L	11 µg/L	6 µg/L	4 µg/L	0 µg/L ^b
SCENARIO 3: 0–1-year-old infant consuming reconstituted baby formula, high consumption					
Assumptions: 1,200 mL/day water consumption [high consumption in EU SCHER (2003)]					
GSD $\frac{1}{4}$ 1.6 µg/dL (IEUBK default value)					
Background exposures from other lead sources set to 0					
10	50 µg/L	32 µg/L	23 µg/L	18 µg/L	13 µg/L
5	20 µg/L	14 µg/L	11 µg/L	9 µg/L	6 µg/L
2	7.3 µg/L	5.3 µg/L	4 µg/L	3.3 µg/L	2.5 µg/L
1	3.5 µg/L	2.5 µg/L	2 µg/L	1.6 µg/L	1.2 µg/L

^aRepetition of Gulson et al.'s (1997) work. All other results reflect additional analyses undertaken herein.

^bDue to other background lead exposures (e.g. air and soil/dust), even 0 µg/L lead in water would still result in exceedance of a given BLL cutoff value.

If the BLL cutoff was set to the new and more stringent level of 5 µg/dL, then 24 µg/L of lead in water is predicted to cause 50% of the population to exceed that BLL cutoff, and 7 µg/L is predicted to cause 25% of the population to exceed the cutoff. However, no WLL is needed to cause exceedance for 10% of the children's population, due to other background lead exposures assumed in the model (Table 3, scenario 1).

Formula-fed infants and lower BLLs

For infants aged 0–1 years consuming the average volume of baby formula milk daily in the presence of other background lead exposures, 60 µg/L of lead in water would elevate the blood lead of 50% of the population, whereas 28 µg/L is predicted to elevate the blood lead of 10% of the population (Table 3, scenario 2). Infants belonging to the upper percentiles (i.e., 25, 10, 5 and 1% in Table 3) reflect more sensitive infants within the exposed population, in comparison to the median response of a typical infant (expressed by the 50th percentile in Table 3). If the BLL cutoff was set at 5 µg/dL, then much lower WLLs would achieve such percentage exceedances for exposed infants consuming formula (Table 3, scenario 2). As expected, reducing the BLL cutoff lowers WLLs of concern to concentrations that were previously considered inconsequential, and below 20 µg/L lead (Table 3, scenario 2).

For infants aged 0–1 years consuming a high dose of baby formula in the absence of any other lead exposure source, even the smallest WLL is predicted to affect some percentage of the population (Table 3, scenario 3). For example, 50 µg/L of lead in water is predicted to elevate lead in blood above 10 µg/dL for 50% of that population, but just 4 µg/L would be enough for 10% of the population to exceed a BLL of 2 µg/dL (Table 3, scenario 3).

While the three modeled scenarios (scenario 1, 2, and 3 in Table 3) are not directly comparable due to the different assumed background lead exposures and GSD in each (see assumptions in Table 3), this analysis demonstrates that a substantial proportion of the 'most sensitive' children within the age group 1–2 years (those in the upper tail of the predicted BLL distribution) may be adversely affected by WLLs much lower than the previously reported WLL of 100 µg/L (Table 3, scenario 1). In addition, consistent

with the Gulson et al. (2004) assertion, formula-fed infants (Table 3, scenarios 2 and 3) are expected to be much more vulnerable to even low-level lead contamination from tap water, due to the large volumes of water required to reconstitute infant formula and due to the high bioavailability factors of infants compared to school-aged children.

It should be noted that the IEUBK model assumptions of (a) log-normal BLL distribution in exposed children (US EPA 2000), and (b) a GSD fixed at the model default value of 1.6 µg/dL (US EPA 2000), or modified to 1.45 µg/dL for formula-fed children (US EPA 2000), are critical to these conclusions. This is because the predicted risk (i.e., % of children exceeding a certain BLL cutoff value) is sensitive to the upper tail of the distribution function. The estimations for the upper tail values would be most affected if these assumptions were not accurate. For example, some previous work challenged the log-normal template of the model when IEUBK predictions were compared to epidemiological data in Polish children (Biesiada & Hubicki 2004). But the key message would remain the same: identifying WLLs that protect the typical child is not an adequate risk assessment approach, and quantified risks to more sensitive subpopulations need to be considered, consistent with the US CDC general policy for environmental contaminants.

Biokinetic modeling of children's BLLs from chronic water exposure at schools

Sathyanarayana et al. (2004) simulated 'typical case' and 'worst case' scenarios of exposure (as termed in that work) to water lead for 71 Seattle elementary schools, yielding relatively low predicted geometric mean BLLs (always <10 µg/dL) for each school, and the authors concluded that 'school drinking water is not likely to contribute to increased BLLs in children' (see Table 1). Reproducing this previous work for children aged 5–6 years, exposed to the 50 and 90th percentile of the combined WLL distribution at one elementary school and at home in Seattle (see Figure 1, combined distribution) yielded a predicted geometric mean BLL of 5.5 µg/dL. Specifically, the geometric mean BLL was 3.3 µg/dL for the previous work's 'typical' water exposure scenario, and 5.5 µg/dL for the previous work's 'worst-case' water scenario at that specific school (Figure 2, tabulated data; all other lead inputs set to IEUBK model default values).

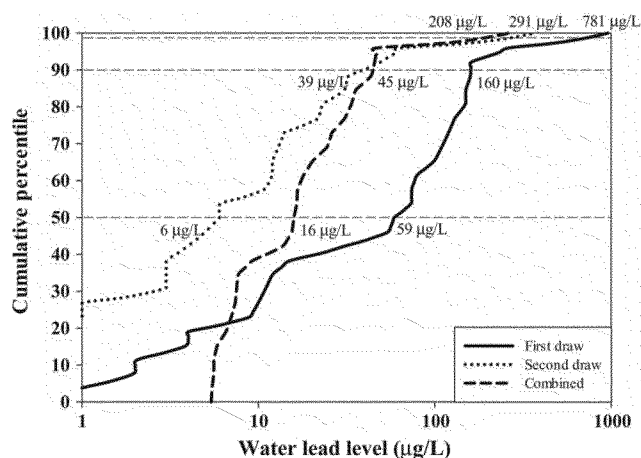


Figure 1 | Percentile lead distribution in first draw, second draw and combined water of a Seattle elementary school in 2004 (i.e., pre-remediation, $n = 29$). The horizontal dashed lines correspond to the 50, 90 and 99th percentile of the measured WLLs in that specific school. (Source of lead-in-water data: Seattle Public Schools (2007).)

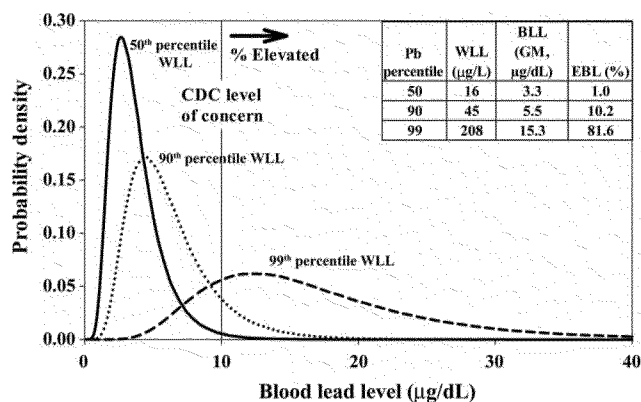


Figure 2 | Predicted log-normal distribution of BLLs in a population of 5–6-year-old students, exposed to the 50, 90 and 99th percentile of combined WLL concentration in a Seattle elementary school in 2004 (IEUBK model).

Overall predicted risk of EBL from water exposure at schools

While evaluating individual WLL inputs and corresponding BLLs is informative, a more formal combination of exposure analysis and dose-response analysis can lead to an overall measure of risk. Children would normally drink from different school taps over the course of a day, so the entire WLL distribution should be considered. This approach is illustrated using the 2004 WLL distribution from one elementary school in Seattle.

From the 71 Seattle elementary schools with publicly available WLLs (Seattle Public Schools [14]), this specific school was selected for this analysis due to the very high WLLs measured in 2004, which caused parental concern during that time. Remedial measures have since been undertaken in this and other Seattle schools, and post-remediation WLLs have now been reported to be much lower (Seattle Public Schools [14]) than the 2004 levels utilized in the historical analysis herein (Figure 1).

Prior to this modeling exercise, the representative WLL distribution needed to be developed. Monitored school first-draw and second-draw WLLs were combined with assumed home WLLs, using the approach of Sathyanarayana et al. [15]. That is, 50% of children's daily water was consumed at school (comprising of 25% first draw and 75% second draw, as measured at a given school). The remaining 50% daily water was consumed at home and was assumed fixed at 10.3 µg/L, equal to the 90th percentile WLL measured in Seattle homes by the drinking water utility (Sathyanarayana et al. [15], see Table 1). Accounting for water lead exposure at home and at school created a combined WLL distribution (Figure 1).

The range of WLL values from this combined distribution were run one-by-one through the IEUBK model, and the corresponding geometric mean BLL output was recorded. The IEUBK biokinetic component thus serves as the dose-response portion of the risk assessment, by relating WLL to BLL (Figure 2, tabulated data). Based on this geometric mean, log-normal distribution assumption, and assumed GSD, the percentage of the exposed population exceeding a given BLL cutoff could also be calculated by the IEUBK model (Figure 2, tabulated data). For example, if water was routinely consumed at the 50th percentile of the combined WLL distribution exposure (i.e., 16 µg/L in Figure 1), a child's predicted likelihood of having EBL based on a 10 µg/dL cutoff is 1.0% (Figure 2, tabulated data). Likewise, exposure to the 90th percentile WLL (i.e., 45 µg/L) corresponds to a 10.2% likelihood of EBL, while exposure to the 99th percentile WLL (i.e., 208 µg/L) corresponds to more than 80% predicted likelihood of EBL (Figure 2, tabulated data). Similar outputs (i.e., % EBL) could be obtained for other BLL cutoffs (e.g., the newly proposed 5 µg/dL). At the new BLL reference value of 5 µg/dL, the respective population exceedance would be 19.2% at

median water lead exposure, 58.1% at the 90% water lead exposure and 99.1% at the 99% water lead exposure (data not shown).

The percentage of exposed children's population exceeding a BLL cutoff for the range of WLLs could then be plotted for two example BLL cutoff values: 10 and 5 $\mu\text{g}/\text{dL}$ (Figure 3(a)). By numerically integrating the area under each curve over the entire distribution of WLLs (see Figure 3(a)), the overall predicted risk of EBL for the students at this school could be calculated. For the previous BLL of concern of 10 $\mu\text{g}/\text{dL}$ this risk was calculated to be

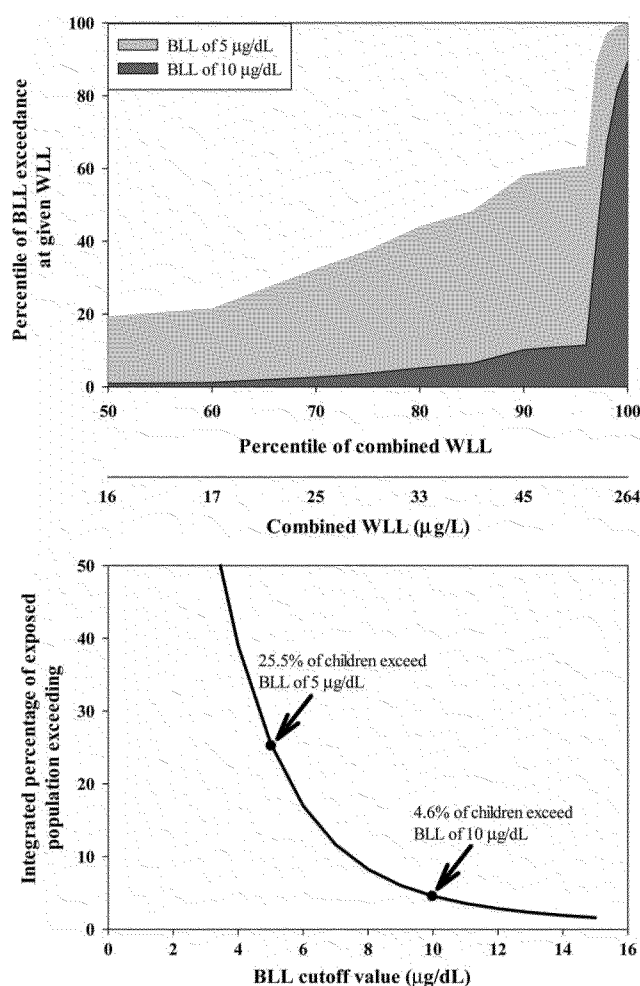


Figure 3 | Predicted percentage of children with elevated blood lead at distinct levels of water lead exposure observed in a Seattle elementary school in 2004 based on IEUBK model (Figure 3(a)). The combined WLL ($\mu\text{g}/\text{L}$) corresponding to each percentile is given on the secondary x-axis (Figure 3(a)). Integration of the curves (i.e., calculation of highlighted area under the curves in Figure 3(a)) estimates overall percentage exceedances depending on the chosen BLL cutoff value, for this historical case study (Figure 3(b)).

4.6% (dark-shaded area in Figure 3(a)). While such a risk is not indicative of an epidemic, parents and health experts would consider it worrisome that 5 out of 100 students attending classes in that specific school are predicted to develop EBL from drinking water consumption. For the new BLL reference value of 5 $\mu\text{g}/\text{dL}$, the corresponding risk was calculated to be 25.5% (the lighter gray shaded area in Figure 3(a)). This methodology was recently used by the authors to assess risk before and after remediation of lead in drinking water at many other elementary schools of Seattle and Los Angeles (Triantafyllidou et al. [11]).

This process can be extended to a range of BLL cutoffs from 2 to 15 $\mu\text{g}/\text{dL}$ (Figure 3(b)). As expected, higher BLL cutoffs have a corresponding low risk, with very few children from the whole school exceeding the high BLL cutoff (Figure 3(b)). However, if the BLL cutoff is set at an even lower level of 2 $\mu\text{g}/\text{dL}$, then 83.5% of students attending classes in that school are predicted to exceed the cutoff value (Figure 3(b)). Overall, lowering the BLL cutoff resulted in non-linear increase in the estimated percentage of children with EBL at one Seattle elementary school in this 2004 historical analysis (Figure 3(b)).

Biokinetic modeling of children's BLLs from acute water exposure

Simulated acute exposure to contaminated water or to food cooked with that water

Preliminary modeling with the ICRP model suggests that one-time exposure of a 5-year old child to a single cup of water (i.e., 250 mL) containing high levels of lead can markedly raise the predicted lead in blood (Figure 4). Such levels of lead in water that elevate lead in blood from a one-time dose have been reported in numerous US field investigations, as summarized by Triantafyllidou & Edwards [12]. These high levels were typically associated with particulate (rather than soluble) lead in water and indeed caused elevated lead in blood of some exposed individuals (Triantafyllidou & Edwards [12]).

Food that requires large volumes of water for cooking can also concentrate lead from the water. This exposure pathway, which has never been assessed in existing blood lead models, has the potential to increase blood lead of children through

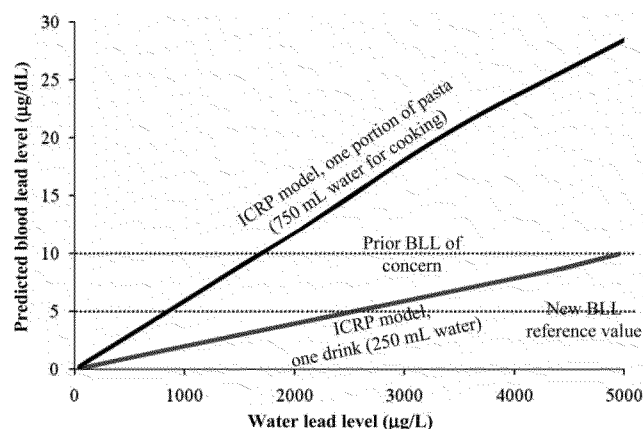


Figure 4 | Predicted blood lead level of 5-year-old-child after direct consumption of lead-contaminated water or consumption of food cooked with that water. The ICRP biokinetic model was employed to predict maximum BLLs from one-time exposures.

consumption of a single food portion, when assuming that 100% of the lead present in water would sorb to the cooked food (Figure 4). Such a pathway was involved in isolated cases of childhood lead poisoning due to food consumption, when tap water was reportedly not consumed directly (Copeland [2000](#); Triantafyllidou & Edwards [2010](#)).

The predictions of the ICRP model from acute water exposures (Figure 4) should be viewed with caution, because the ICRP model was shown to overestimate BLLs for similar chronic exposure scenarios in children, when compared to the IEUBK model (US EPA [2000b](#)). In addition, it is possible that not all lead found in water will sorb to cooked food, as was assumed here. Nonetheless, the point of this analysis is that modeling acute exposures and cooking with contaminated water can provide useful insights for the risk assessment of lead in water, that were not previously considered. Because some lead in water may sorb onto cooked food, source-apportionment analyses should consider both direct drinking water consumption and indirect dietary impacts.

Applying the US CPSC lead acute health dose to water

If the US CPSC dose of acute health concern in children's lead jewelry (175 µg lead in one piece of ingested jewelry as described in the Introduction) was applied to lead detected in water, then the one-time ingestion of 250 mL of water containing 700 µg/L lead would result in an equal lead dose of 175 µg [i.e., $(0.250 \text{ L}) \times (700 \text{ µg/L}) = 175 \text{ µg}$] and therefore

must also be considered an acute health risk to children. Similarly, a one-time consumption of pasta cooked with 750 mL water containing 233 µg/L of lead, would result in a lead dose of 175 µg [i.e., $(0.750 \text{ L}) \times (233 \text{ µg/L}) = 175 \text{ µg}$] and pose an acute health concern if all the lead was captured in the food. While water lead levels of 233 µg/L, 700 µg/L or higher are relatively rare, they have been detected in worst-case Seattle schools (e.g., in the school examined in this study) and other US schools or homes (Triantafyllidou & Edwards [2010](#)), and could cause an acute health concern.

LIMITATIONS

Limitations of existing models apply not only to the work presented here, but also to results of previous research. Specifically, potential limitations of the ICRP and IEUBK models have been reported elsewhere (Pounds & Leggett [2000](#); US EPA [2000b](#); Equilibrium Environmental Inc. [2000](#)). The numerical results presented in this paper are based on certain modeling assumptions, and it is recognized that different assumptions would result in different results. For example, Donohue et al. ([2000](#)) proposed different default input values (e.g., for daily water consumption), compared to the IEUBK default values used here. It is also recognized that the ability of the IEUBK model to predict the 'tail' of the BLL distribution is limited, which is why previous research was justified in restricting conclusions to the typical case (i.e., predictions of geometric mean BLL only).

In addition, the high WLLs used in ICRP simulations are typically associated with particulate lead presence in tap water, which may be less bioavailable compared to the ICRP model default bioavailability factor of 30% for oral ingestion of lead. However, recent work by Deshommes & Prévost ([2010](#)) on particulate lead suggests that this bioavailability factor is reasonable. Regardless of potential limitations, the general trends reported here reflect predictions based on available modeling tools.

CONCLUSIONS

Repetition of previous modeling work is consistent with the expectation that lead in tap water is not a major risk for a

typical child under chronic exposure scenarios when applying a 10 µg/dL BLL for health concerns.

Considering the whole predicted distribution of BLLs (log-normal with a GSD of 1.6 µg/dL in the IEUBK model) and not just the geometric mean BLL for a population exposed to a fixed WLL, reveals significant health impacts for the most sensitive children at the upper tail of the distribution, even at low levels of water lead. From a risk assessment perspective, the upper tail of the BLL distribution is critical in defining risk. This is because it allows estimating the percentage of children predicted to exceed a certain BLL cutoff value, due to variations in genetics and diets that render them more sensitive compared to other children in that population.

Explicit consideration of formula-fed infants, who are a high-risk group due to their small body weight and heavy reliance on water as a major component of their diet, also revealed significant health concerns at relatively low WLLs (<50 µg/L). Investigating children's lead exposure at one elementary school in Seattle, and acknowledging that children are exposed to an entire distribution of WLLs, led to a 4.6% overall predicted risk of BLL \geq 10 µg/dL in children attending classes in that school in 2004 (pre-remediation), and 25.5% overall predicted risk of BLL \geq 5 µg/dL.

Expanding previous modeling analyses to consider lower BLL cutoff values (e.g., 5, 2, and 1 µg/dL versus 10 µg/dL) is consistent with increased public health concern about low level lead exposure, and indicated that relatively low WLLs (<24 µg/L) would have an adverse impact for high-risk groups (i.e., very young children and formula-fed infants). A reduction in the BLL reference value from 10 to 5 µg/dL also lowers the WLL of concern below 20 µg/L for certain high-risk subpopulations.

Finally, acute exposures from direct water consumption or food cooked with contaminated water at the upper range of WLLs encountered in US school sampling events, have a potential to cause blood lead elevations \geq 10 µg/dL or \geq 5 µg/dL in children.

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